REMARKS/ARGUMENTS

The Pending Claims

Claims 22, 25, 26, and 28 are pending and are directed to a method for screening for a molecule that modulates gamma-secretase activity.

The Amendments to the Specification and Claims

The specification has been amended to insert a degree symbol between "65" and "C" on page 28. Claims 1-20, 29-40, and 42-48 have been cancelled as being drawn to non-elected inventions. Applicants reserve the right to pursue any cancelled subject matter in a continuation, continuation-in-part, divisional, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter. Claim 22 has been rewritten in independent form and has been amended to recite a method for screening for a molecule that modulates gamma-secretase activity. This amendment is supported by the specification at, e.g., page 61, lines 16-22, and by original claim 8. Claims 25, 26, and 28 have been amended to correct matters of form. Claim 28 also has been amended to recite that the candidate molecule is a drug for treatment or prevention of Alzheimer's disease. This amendment is supported by the specification at, e.g., page 18, lines 20-25. Claims 21, 27, and 49 have been cancelled. Thus, no new matter has been added by way of these amendments.

The Office Action

The Office Action objects to the specification because the degree sign in "65 C" on page 28 allegedly is missing. The Office Action objects to claims 21-28 and 49 because these claims depend from claim 1 or claim 9, which are non-elected claims.

The Office Action rejects claims 21-28 and 49 under 35 U.S.C. § 101, because the invention defined by these claims is allegedly not supported by either a specific and substantial asserted utility or a well-established utility. The Office Action rejects claims 21-28 and 49 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement and written description. The Office Action rejects claims 21-28 and 49 under 35 U.S.C. § 112, second

paragraph, as allegedly indefinite. Claim 49 is rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent 6,913,919 ("the '919 patent").

Reconsideration of these objections and rejections is respectfully requested.

Discussion of Objections

The objections to the specification and claims have been rendered moot as a result of the amendments to the specification and claims discussed above.

Discussion of Rejection Under 35 U.S.C. § 101

The Office Action rejects claims 21-28 and 49 under Section 101 as allegedly lacking a specific and substantial utility or a well-established utility. Applicants note that claims 21, 27, and 49 have been cancelled, and the rejection will be addressed as it pertains to claims 22, 25, 26, and 28.

The Office Action contends that the specification does not disclose any specific biological significance for the protein complex recited in the claims, or its relevance to a particular disease. In addition, the Office Action contends that the specification does not provide any evidence that supports that a complex of sambiasin-1, presenilin-1, and nicastrin is associated with any disease or disorder, and does not provide a nexus between this complex and Alzheimer's disease or disorders associated with aberrant Notch signaling.

Evidence of pharmacological or other biological activity of a compound is relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. *Cross v. Iizuka*, 753 F.2d. 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d. 1322, 206 U.S.P.Q 885 (C.C.P.A. 1980); *Nelson v. Bowler*, 626 F.2d. 853, 206 U.S.P.Q. 881 (C.C.P.A. 1980). An applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of a compound or composition, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof. The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does the applicant have to provide actual evidence of success in treating humans where such a utility is asserted. M.P.E.P. § 2107.03.

The specification discloses that protein complexes comprising presenilin and nicastrin play a role in controlling gamma-secretase activity, which has been implicated in the development of amyloid plaques in Alzheimer's disease, as well as disorders caused by defects in the Notch signaling pathway (see specification at, e.g., page 2, first paragraph). As such, the disclosed complex comprising sambiasin-1, presenilin-1, and nicastrin can be used to identify compounds that interact with the complex and thereby modulate gamma-secretase activity (see specification at, e.g., page 19, lines 5-8, and page 61, lines 14-32).

The specification (see, e.g., page 1, third paragraph) as well as the prior art (see, e.g., Li et al., *Proc. Natl. Acad. Sci. USA*, 97: 6138-6143 (2000) ("the Li reference")) discloses that aberrant cleavage of beta amyloid precursor protein is believed to be one of the main causes of Alzheimer's disease. This cleavage is due to gamma-secretase activity. The specification discloses a subclass of gamma-secretase modulators, namely those which bind to the protein complex recited in claim 22. The Li reference discloses that gamma-secretase is part of a high molecular weight complex comprising presenilin. The Li reference further demonstrates that solubilized gamma-secretase activity coelutes with presenilin-1 (PS1) at an apparent molecular weight of approximately 2.0×10^6. In addition, anti-PS1 antibody immunoprecipitates gamma-secretase activity from a solubilized gamma-secretase preparation. These data suggest that gamma-secretase activity is catalyzed by a PS-1 containing macromolecular complex. The specification demonstrates for the first time that this PS1 protein complex also comprises Sambiasin-1 and Nicastrin. Consequently, molecules which bind to a complex comprising these proteins and which modulate gamma-secretase activity are candidates for the treatment of Alzheimer's disease.

In view of the foregoing, Applicants submit that the aforementioned utilities are specific, substantial, and credible as prescribed in M.P.E.P. § 2107.01. Accordingly, Applicants request the withdrawal of the rejection under Section 101.

Discussion of Enablement Rejection

The Office Action rejects claims 21-28 and 49 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Applicants note that claims 21, 27, and 49 have been cancelled, and the rejection will be addressed as it pertains to claims 22, 25, 26, and 28.

Specifically, because the pending claims allegedly lack utility, the Office Action alleges that one of ordinary skill in the art allegedly would not know how to make and use the claimed invention. In addition, the Office Action alleges that the specification does not provide guidance as to the specific structures of the functionally active fragments, derivatives, homologs, or variants of sambiasin-1, presenilin-1, or nicastrin that are required to maintain the claimed protein complex.

The Office Action, however, acknowledges that the specification enables a protein complex comprising sambiasin-1, presenilin-1, and nicastrin, as well as a method for identifying a molecule that binds to the protein complex to affect activity of the complex (Office Action at page 11, second paragraph).

As discussed above with respect to the Section 101 rejection, claims 22, 25, 26, and 28 involve a specific, substantial, and credible utility. Solely in an effort to advance the prosecution of the application, and not in acquiescence of the rejection, claim 22 has been amended to recite a method for screening for a molecule that modulates gamma-secretase activity, comprising (a) exposing a protein complex comprising (i) Sambiasin-1 (SEQ ID NO: 1), (ii) Presenilin-1 (SEQ ID NO: 2), and (iii) Nicastrin (SEQ ID NO: 3) to one or more candidate molecules; and (b) determining the gamma-secretase activity of the complex. Claim 22 no longer refers to functionally active fragments, derivatives, homologs, or variants of sambiasin-1, presenilin-1, or nicastrin.

For the foregoing reasons, the specification enables the invention defined by claims 22, 25, 26, and 28. As such, the enablement rejection under Section 112, first paragraph, should be withdrawn.

Discussion of Written Description Rejection

The Office Action rejects claims 21-28 and 49 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. Applicants note that claims 21, 27, and 49 have been cancelled, and the rejection will be addressed as it pertains to claims 22, 25, 26, and 28.

The Office Action contends that the claims are broadly directed to a method of using a genus of protein complexes comprising functional fragments, derivatives, homologs, or variants, yet the specification does not describe the entire genus of proteins. The Office

Action acknowledges, however, that the application adequately describes a protein complex comprising sambiasin-1 and presenilin-1 molecules for use in the claimed method. The Office Action further alleges that a representative number of species must be described in order to claim possession of the entire genus.

Solely in an effort to advance prosecution of the application, and not in acquiescence of the rejection, claim 22 has been amended to recite a method for screening for a molecule that modulates gamma-secretase activity, comprising (a) exposing a protein complex comprising (i) Sambiasin-1 (SEQ ID NO: 1), (ii) Presenilin-1 (SEQ ID NO: 2), and (iii) Nicastrin (SEQ ID NO: 3) to one or more candidate molecules; and (b) determining the gamma-secretase activity of the complex. Claim 22 no longer refers to functionally active fragments, derivatives, homologs, or variants of sambiasin-1, presenilin-1, or nicastrin.

For the foregoing reasons, the specification adequately describes the invention defined by claims 22, 25, 26, and 28. As such, the written description rejection under Section 112, first paragraph, should be withdrawn.

Discussion of Indefiniteness Rejection

The Office Action rejects claims 21-28 and 49 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. This rejection is traversed for the reasons set forth below.

The Office Action contends that claims 21 and 49 are incomplete for omitting a detecting step to determine whether the candidate molecule is bound to the complex. Claim 22 allegedly is incomplete for omitting a detecting step to determine and evaluate the activity or function of the complex. Claims 22-28 and 49 also are allegedly indefinite due to certain vague terms recited therein (e.g., "function," "activity," and "change"). Claims 22-28 are further allegedly indefinite because the functionally active fragments, derivatives, homologs, or variants of sambiasin-1, presenilin-1, or nicastrin are not defined in the specification. In addition, the Patent Office alleges that the specification does not define what is meant by "developmental disorders caused by a defect in the Notch pathway."

Solely in an effort to advance prosecution of the application, and not in acquiescence of the rejection, claims 21 and 49 have been cancelled. Claim 22 has been amended to recite a step in which the gamma secretase activity of the protein complex is determined after the

complex is exposed to one or more molecules that may modulate gamma secretase activity. Claim 22 also has been amended to delete the terms "function" and "change," and to no longer refer to functionally active fragments, derivatives, homologs, or variants of sambiasin-1, presenilin-1, or nicastrin. The term "gamma-secretase activity" is clearly defined in the specification at, e.g., page 15, lines 20-24. Claim 28 has been amended to recite that the candidate molecule is a drug for treatment or prevention of Alzheimer's disease.

In view of the foregoing, the metes and bounds of claims 22, 25, 26, and 28 are clear, and the rejection under Section 112, second paragraph, should be withdrawn.

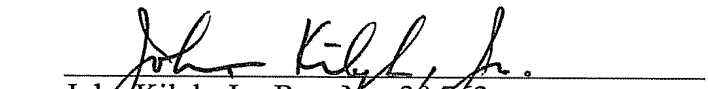
Discussion of Anticipation Rejection

Claim 49 is rejected under 35 U.S.C. § 102(e) as allegedly anticipated by the '919 patent. Claim 49 has been cancelled, thereby mooting this rejection. Applicants further note that the '919 patent does not disclose or suggest the subject matter of claim 22, 25, 26, or 28, as amended.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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